Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	5	Judy Raucy	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/04/14 12:55
S2	673	cyp3a4	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/04/14 12:29
S3	266	pxr	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/04/14 12:25
S4	4	pxre	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/04/14 12:26
S5	9	xrem	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/04/14 12:26
S6	3	S2 and S3 and S4 and S5	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/04/14 12:26
S7	834	cyp3a$	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/04/14 12:27
S8	9	S5 and (S3 or S5 or S4)	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/04/14 12:27
S9	133	S2 and P-450	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/04/14 12:29
S10	86	cyp3a4.clm.	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/04/14 12:29
S11	2	"20020168623"	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/04/14 12:55
S12	1	S11 and (endogenous chromosome)	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/04/14 12:56

S13	1	S11 and (endogenous chromosome) and reporter NEAR gene	US-PGPUB; USPAT; EPO; JPO; DERWENT	NEAR	ON	2005/04/14 12:56

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=> d his

     (FILE 'HOME' ENTERED AT 14:27:36 ON 14 APR 2005)

     FILE 'MEDLINE, CANCERLIT, AGRICOLA, CAPLUS, SCISEARCH' ENTERED AT
     14:27:46 ON 14 APR 2005
                E RAUCY J?/AU
L1            20 S E4
L2            36 S E1
L3            36 S E1
L4            46 S E5
L5           102 S L1 OR L2 OR L3 OR L4
L6          7899 S CYP3A4
L7            23 S PXRE
L8          1282 S PXR
L9            30 S XREM
L10            0 S L6 (L) L7 (L) L8 (L) L9
L11          265 S L6 (L) L8
L12           21 S L11 AND (PXRE OR XREM)
L13            9 DUP REM L12 (12 DUPLICATES REMOVED)
L14            9 SORT L13 PY
L15           23 S L5 AND L6
L16           14 DUP REM L15 (9 DUPLICATES REMOVED)
L17           14 SORT L16 PY
L18           14 FOCUS L17 1-

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L18 ANSWER 5 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:490332 CAPLUS
DN 141:48496
TI Reporter gene systems for the identification of compounds inducing genes of xenobiotic and drug metabolism
SO U.S. Pat. Appl. Publ., 52 pp., Cont.-in-part of U.S. Ser. No. 832,621.
CODEN: USXXCO
IN **Raucy, Judy**
AB Reporter gene systems that are inducible by xenobiotics are described for use in the screening of xenobiotics and drugs for their ability to induce expression of genes for xenobiotic or drug metabolism In particular, the method is used to screen for inducers of expression of the gene for cytochrome **CYP3A4**. The system uses a gene for a receptor or transcription factor responsive to xenobiotics and a reporter gene under control of a promoter regulated by the receptor or transcription factor. The method can also be used to assay the effectiveness of a compound, such as a drug, as an inducer of expression from xenobiotic-dependent promoters. This method can be adapted to high throughput screening. Use of the promoter of the **CYP3A4** gene to drive expression of a luciferase reporter gene is demonstrated. The gene was inducible by xenobiotics including TCDD and a number of dietary flavonoids.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004115627	A1	20040617	US 2002-222679	20020816
WO 2001079845	A1	20011025	WO 2001-US11819	20010411
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002168623	A1	20021114	US 2001-832621	20010411
WO 2004016759	A2	20040226	WO 2003-US25619	20030815
WO 2004016759	A3	20040401		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004077080	A1	20040422	US 2003-642322	20030815

L18 ANSWER 13 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:331687 CAPLUS
DN 140:351644
TI Reporter gene systems for the identification of compounds inducing genes of xenobiotic metabolism
SO U.S. Pat. Appl. Publ., 91 pp., Cont.-in-part of U.S. Ser. No. 222,679.
CODEN: USXXCO
IN **Raucy, Judy**
AB Transgenic cells which may be used to test xenobiotics for induction of genes encoding xenobiotic-metabolizing enzymes are disclosed. The system uses a gene for a receptor or transcription factor responsive to xenobiotics and a reporter gene under control of a promoter regulated by the receptor or transcription factor. This method can be adapted to high throughput screening. Thus, HepG2 and Caco2 cell lines were stably transformed with a vector encoding PXR as well as another vector containing the firefly luciferase gene under control of PXR-binding MDR1 promoter elements. Luciferase gene induction was observed in response to rifampicin, dexamethasone, mevastatin, mifepristone, omeprazole, kava-kava, chrysin, 2-AAF, and methoxychlor.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI US 2004077080	A1	20040422	US 2003-642322	20030815
US 2002168623	A1	20021114	US 2001-832621	20010411
US 2004115627	A1	20040617	US 2002-222679	20020816

L18 ANSWER 14 OF 14 CAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:162791 CAPLUS
DN 140:212007
TI Reporter gene systems for the identification of compounds inducing genes of xenobiotic metabolism
SO PCT Int. Appl., 160 pp.
CODEN: PIXXD2
IN **Raucy, Judy**
AB Reporter gene systems that are inducible by xenobiotics are described for use in the screening of xenobiotics for their ability to induce gene expression. The system uses a gene for a receptor or transcription factor responsive to xenobiotics and a reporter gene under control of a promoter regulated by the receptor or transcription factor. The method can also be used to assay the effectiveness of a compound, such as a drug, as an inducer of expression from xenobiotic-dependent promoters. This method can be adapted to high throughput screening.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2004016759	A2	20040226	WO 2003-US25619	20030815
WO 2004016759	A3	20040401		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004115627	A1	20040617	US 2002-222679	20020816

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L14 ANSWER 1 OF 9 MEDLINE on STN
AN 2000398102 MEDLINE
TI Dexamethasone induces pregnane X receptor and retinoid X receptor-alpha expression in human hepatocytes: synergistic increase of CYP3A4 induction by pregnane X receptor activators.
SO Molecular pharmacology, (2000 Aug) 58 (2) 361-72.
Journal code: 0035623. ISSN: 0026-895X.
AU Pascussi J M; Drocourt L; Fabre J M; Maurel P; Vilarem M J
AB In this report we show that submicromolar concentrations of dexamethasone enhance pregnane X receptor (**PXR**) activator-mediated **CYP3A4** gene expression in cultured human hepatocytes. Because this result is only observed after 24 h of cotreatment and is inhibited by pretreatment with cycloheximide, we further investigated which factor(s), induced by dexamethasone, might be responsible for this effect. We report that dexamethasone increases both retinoid X receptor-alpha (RXRalpha) and **PXR** mRNA expression in cultured human hepatocytes, whereas **PXR** activators such as rifampicin and clotrimazole do not. Accumulation of RXRalpha and **PXR** mRNA reaches a maximum at a concentration of 100 nM dexamethasone after treatment for 6 to 12 h and is greatly diminished by RU486. A similar pattern of expression is observed with tyrosine aminotransferase mRNA. Moreover, the effect of dexamethasone on **PXR** mRNA accumulation seems to be through direct action on the glucocorticoid receptor (GR) because the addition of cycloheximide has no effect, and dexamethasone does not affect the degradation of **PXR** mRNA. Furthermore, dexamethasone induces the accumulation of a RXRalpha-immunoreactive protein and increases the nuclear level of RXRalpha:**PXR** heterodimer as shown by gel shift assays with a **CYP3A4** ER6 **PXRE** probe. This accumulation of latent **PXR** and RXRalpha in the nucleus of hepatocytes explains the synergistic effect observed with dexamethasone and **PXR** activators together on **CYP3A4** induction. These results reveal the existence of functional cross talk between the GR and **PXR**, and may explain some controversial aspects of the role of the GR in **CYP3A4** induction.

L18 ANSWER 3 OF 14 MEDLINE on STN
AN 2004631765 IN-PROCESS
TI High volume bioassays to assess **cyp3a4**-mediated drug interactions: induction and inhibition in a single cell line.
SO Drug metabolism and disposition: biological fate of chemicals, (2005 Jan) 33 (1) 38-48. Electronic Publication: 2004-10-01.
Journal code: 9421550. ISSN: 0090-9556.
AU Yueh Mei-Fei; Kawahara Marleen; **Raucy Judy**
AB Exposure to certain xenochemicals can alter the catalytic activity of the major drug-metabolizing enzyme, **CYP3A4**, either by enhancing expression of this cytochrome P450 or inhibiting its activity. Such alterations can result in adverse consequences stemming from drug-drug interactions. A simplified and reliable tool for detecting the ability of candidate drugs to alter **CYP3A4** levels or inhibit catalytic activity was developed by stable integration of human pregnane X receptor and a luciferase vector harboring the **CYP3A4** enhancers. Treatment of stable transformants, namely DPX-2, with various concentrations of inducers including rifampicin, mifepristone, troglitazone, methoxychlor, and kava produced dose-dependent increases in luciferase expression (between 2- and 40-fold above dimethyl sulfoxide-treated cells). Northern blot analyses of **CYP3A4** mRNA in DPX-2 cells exhibited a good correlation to results generated with the reporter gene assay ($r(2) = 0.5$, $p < 0.01$). Induction of **CYP3A4** protein was examined by measuring catalytic activity with the **CYP3A4** substrate, luciferin 6' benzyl ether (luciferin BE). Metabolism of luciferin BE by DPX-2 cells was enhanced 5.2-fold above dimethyl sulfoxide-treated cells by treatment with rifampicin. Constitutive androstane receptor-mediated regulation of **CYP3A4** protein was addressed by measuring catalytic activity in a separate cell line over-expressing this receptor. Phenobarbital and dexamethasone produced 1.5- and 2.0-fold increases, respectively, above control in luciferin BE metabolism. To determine the utility of DPX-2 cells for identifying inhibitors of **CYP3A4** catabolism, luciferin BE activity was measured in the presence of various concentrations of ketoconazole, erythromycin, or kava. These agents exhibited dose-dependent decreases in **CYP3A4** activity with IC(50) values of 0.3 microM for ketoconazole, 108 microM for erythromycin, and 15.5 microg/ml for kava. Collectively, DPX-2 cells were used to identify xenobiotics that induce or inhibit **CYP3A4** in a high throughput manner, demonstrating their applicability to early-stage drug development.

L18 ANSWER 4 OF 14 MEDLINE on STN
AN 2002482973 MEDLINE
TI A cell-based reporter gene assay for determining induction of **CYP3A4** in a high-volume system.
SO Journal of pharmacology and experimental therapeutics, (2002 Oct) 303 (1) 412-23.
Journal code: 0376362. ISSN: 0022-3565.
AU **Raucy Judy**; Warfe Lyndon; Yueh Mei-Fei; Allen Scott W
AB Assessing the inducibility of **CYP3A4** by various xenobiotics can predict potential drug interactions. In the present investigation, human hepatoma cells were stably integrated with either the **CYP3A4** enhancer region and a luciferase reporter gene or the **CYP3A4** -luciferase construct and the human pregnane X receptor (PXR). Several colonies containing one to three copies of luciferase per cell were identified by Southern blot analysis. Those transformants producing high luciferase activity in response to rifampicin were used to standardize a 96-well plate screening system with minimal inter- and intraplate variability. Standardization also consisted of assessing viability of cells cultured in medium containing various serum concentrations. In cells maintained for 48 h in medium with less than 5% serum, a significant ($p < 0.01$) decline was observed in viability accompanied by altered induction. A defined serum-free medium also produced less viable cells but did not alter the inductive response. Treatment of transformants with various concentrations of rifampicin produced a dose-response curve with maximal induction at 10 microM (5.6 +/- 0.18- and 2.1 +/- 0.3-fold above dimethyl sulfoxide (DMSO)-treated cells in transformants with and without PXR, respectively). Of additional agents examined for their ability to induce **CYP3A4**, omeprazole (200 microM) was the most potent inducer (12.8 +/- 1.9- and 2.4 +/- 0.2-fold above DMSO-treated cells in transformants with and without PXR, respectively). Mifepristone and mevastatin produced modest induction (approximately 3-fold) in the cell line containing exogenous PXR, but produced less than 1.2-fold increases in cells lacking PXR. Thus, only potent inducers can be identified in the cell line without PXR. In contrast, cells containing the receptor can be used to rank **CYP3A4** induction. Because a high volume of chemicals can be readily and accurately screened for their ability to induce **CYP3A4** with this format, such a system could be valuable in the initial stages of preclinical drug development.